REMARKS

Claims 1, 3-13, 19-21, and 23-25 are pending and under consideration, prior to Amendment.

Applicants cancel, without prejudice, claims 10-13, 19, and 20, which were previously withdrawn from consideration as directed to a non-elected invention. Additionally, Applicants cancel, without prejudice, claim 3.

Applicants add new claims 26-60. Support for the subject matter of the newly added claims is found throughout the specification. No new matter has been added. Support for claims 26-33 and 60 can be found, for example, in the claims as filed; in paragraphs [0023], [0024], and [0544] of the published specification; and in Examples 2, 5, 6, 7, and 8. Support for claims 34-39 can be found, for example, in paragraphs [0024] and [0027] of the published specification. Support for claims 40-59 can be found, for example, in paragraphs [0543] and [0544] of the published specification.

Claim 1 has been amended to more particularly point out that the *hedgehog* antibody *binds to Sonic hedgehog protein and inhibits hedgehog signaling*. Support for Applicants' amendment can be found, for example, in paragraphs [0498]-[0501], [0723], and [0725]-[0729] of the published specification. Claim 1 has also been amended to point out that the unwanted cell proliferation is *associated with cancer* and that the cancer *is associated with one or more of prostate, breast, bladder, or colon tissue* (the amendment incorporates the features of claims 3 and 5). Support for Applicants' amendment can be found, for example, in the previously pending claims; in paragraph [0544] of the published specification; and in Examples 2, 5, 6, 7, and 8. Claim 1 has also been amended to correct a typographical error regarding the term "overexpress".

Claim 21 has been amended to more particularly point out that the *hedgehog* antibody *binds to Sonic hedgehog protein and inhibits hedgehog signaling*. Support for Applicants' amendment can be found, for example, in paragraphs [0498]-[0501], [0723], and [0725]-[0729] of the published specification.

Claims 5, 23, and 24 have been amended to correct claim dependencies and to more particularly point out the tissues with which cancer is associated.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the Office Action mailed September 11, 2007.

Continued Examination Under 37 CFR 1.114

Applicants note with appreciation that the finality of the previous Office Action has been withdrawn in view of Applicants' Request for Continued Examination.

Withdrawn Objections and/or Rejections

Applicants note with appreciation the withdrawal of certain objections and rejections.

Maintained Objections and/or Rejections

Claim Rejections – 35 § USC 112, 1st paragraph, written description

Claims 1-3, 5, 21, and 23-25 are rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the written description requirement. Applicants traverse this rejection and contend that the rejection is moot in view of the amended claims.

The basis of this rejection is that Applicants have allegedly failed to describe the entire genus of *hedgehog* antibodies. A review of the Examiner's rejection indicates that the rejection is based on the Examiner's interpretation of the genus of *hedgehog* antibodies. Specifically, the Examiner interprets the term "hedgehog antibody" to encompass antibodies to "any member of the hedgehog family", as well as to "any member of the hedgehog signaling pathway (including gli-1, gli-2, gli-3, patched, smoothened, and other undisclosed components of the pathway)." See page 3 of the Office Action.

Applicants respectfully disagree with the Examiner's interpretation of the term "*hedgehog* antibody" as encompassing antibodies against any component of the *hedgehog* signaling pathway. Nevertheless, to expedite prosecution, Applicants have amended the claims to more particularly point out that the *hedgehog* antibody binds to Sonic hedgehog protein and inhibits *hedgehog* signaling (e.g., the *hedgehog* antibody is an anti-*Sonic hedgehog* antibody). Applicants' amendment is not in acquiescence to the rejection. Applicants reserve the right to prosecute claims of similar or differing scope.

Applicants' amendment serves to clarify the claims by more particularly pointing out the structure and function of the *hedgehog* antibodies for use in the claimed method. Specifically, the

hedgehog antibody is described structurally and functionally as binding to Sonic hedgehog protein (e.g., the antibody is described with reference to its antigen) and inhibiting *hedgehog* signaling. Applicants' contention that the *hedgehog* antibodies for use in the claimed methods are described in compliance with 35 U.S.C. 112, first paragraph, is supported by the Federal Circuit's finding in *The Regents of the University of California v. Eli Lilly and Co.*, as clarified by *Enzo Biochem, Inc. v. Gen-Probe, Inc. The Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 1997); *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316 (Fed. Cir. 2002). Although *Lilly* and *Enzo* dealt with how to adequately describe a genus of biological materials in the context of a claim directed to the biological material itself, certain principals detailed in these cases are applicable to the instant case.

In outlining that which constitutes an adequate description of a genus with respect to genetic material, the court asserted that adequate description requires more than the gene or protein name.

> "[A] cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the DNA. See Fiers, 984 F.2d at 1171, 25 U.S.P.Q.2D (BNA) at 1606. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus **or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."** (emphasis supplied) 119 F.3d at 1566

Accordingly, for the description of a genetic invention to be deemed adequate to describe the genus that the claims encompass requires **either** a recitation of the structure of a representative number of members of the genus **or** a recitation of the common features of the members of the claimed genus.

The court in *Enzo* further clarified that "*Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement." *Enzo Biochem, Inc.*, 296 F.3d at 1328. The court found that the claims satisfied the written description requirement despite the fact that neither the specification nor the deposited biological material recited the structure, formula, chemical name, or physical properties of the material.

Applicants submit that the pending claims define the claimed subject matter in terms of generic formulae that indicate with specificity what the generic claims encompass, and accordingly meet the guidelines set forth above and comply with the written description requirement. The *hedgehog* antibodies for use in the claimed methods are described based on **both** structural **and** functional characteristics. Accordingly, one of skill in the art can readily envision the *hedgehog* antibodies for use in the claimed methods.

The specification and the state of the art further support Applicants' contention that the *hedgehog* antibodies for use in the claimed methods are adequately described. The specification and state of the art provide ample guidance such that one of skill in the art can readily envision the structure of a *hedgehog* antibody that binds to Sonic hedgehog protein and inhibits *hedgehog* signaling. For example, the specification provides an example of such an antibody, 5E1. Furthermore, at the time of filing of the instant application, Fujita (1997, Biochemical and Biophysical Research Communication 238: 658-664; previously cited in Applicants' IDS) had used, in an in vitro system, polyclonal antibodies raised to the N-terminal portion of Sonic hedgehog.

The Examiner has cited *Vas-Cath, Inc. v. Mahurkar*, *Fiers v. Revel*, and *Amgen v. Chugai Pharmaceutical Co.*, and has alleged that the claimed invention does not satisfy the written description requirement, as articulated in these cases. Applicants respectfully disagree. As an initial point, as detailed above, Applicants have described the *hedgehog* antibodies for use in the claimed methods in a manner fully compliant with *Lilly*, a decision that quoted *Fiers* when articulating the requirement for adequately describing nucleic acids. Thus, contrary to the Examiner's assertion, Applicants contend that the instant claims are fully compliant with the written description requirement, as set forth in this line of cases.

Additionally, Applicants note that the Examiner has exclusively cited case law relevant to written description of compositions, not methods. In *Capon v. Eshhar*, the Federal Circuit discussed in detail that the written description requirement must be analyzed in the context of the particular invention, technology, and state of the art ("the 'written description' requirement states that the patentee must describe the invention, it does not state that every invention must be described in the same way). *Capon v. Eshhar*, 418 F.3d 1349, 1358 (Fed. Cir. 2005). The claims at issue in *Capon* were directed to chimeric DNAs and expression vectors comprising the chimeric

DNAs. Although the claims at issue in *Capon* were directed to biological compositions, the court still distinguished the factual situation from that of *Lilly*, *Fiers*, and *Amgen*. The court noted that in *Lilly*, *Fiers*, and *Amgen*, the claimed compositions included biological material that was unknown and had not been characterized. *Capon*, 418 F.3d at 1357-1358. In contrast, the compositions in *Capon*, although broadly and generically claimed without reference to particular sequences, were based on combining elements for which known examples existed in the art.

The factual situation in the instant case is more analogous to *Capon* than to *Lilly*, *Fiers*, and *Amgen*. Exemplary monoclonal and polyclonal *hedgehog* antibodies that bind to Sonic hedgehog and inhibit *hedgehog* signaling were already known in the art prior to Applicants' invention. Accordingly, Applicants' claims, which describe the use of such antibodies by reference to both structural and functional features, is unlike an attempt to claim an unknown biological material without reference to its specific sequence. In the present case, one of skill in the art can readily envision that which is claimed.

The position articulated in *Capon* was followed by the Federal Circuit in *Falkner v. Inglis*. *Falkner v. Inglis*, 468 F.3d 1357, 1369 (Fed. Cir. 2006) ("As we stated in *Capon*, the 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way."). *Falkner* additionally held that

> "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure."
> *Falkner*, 467 F.3d at 1367.

Although *Falkner* held that "examples are not necessary to support the adequacy of a written description", the specification and the art at the time of filing did provide examples of *hedgehog* antibodies that bind Sonic hedgehog and inhibit *hedgehog* signaling. Although *Falkner* held that "the written description standard may be met ... even where actual reduction to practice of an invention is absent", the specification and art did provide an actual reduction to practice of a

hedgehog antibody that binds to Sonic hedgehog and inhibits *hedgehog* signaling. Further, the specification advances the state of the art and provides working examples that a *hedgehog* antibody that binds to Sonic hedgehog and inhibits *hedgehog* signaling can be used to inhibit growth of certain tumors. Although *Falkner* held that "there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure", the specification and present claims do describe and recite a known structure. The *hedgehog* antibodies are described structurally and functionally based on the ability to bind to Sonic hedgehog (antigen) and inhibit *hedgehog* signaling. Further, the sequence and structure of the antigen (Sonic hedgehog) was well known in the art at the time of filing. Thus, Applicants contend that the instant specification goes well beyond that which is required to satisfy the written description requirement.

Applicants' position does not represent a change in the law. "The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Moba v. Diamond Automation, Inc.*, 325 F.3d 1306, 1322 (Fed. Cir. 2003) (citing *Union Oil Co. of Cal. v. Altantic Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000)). The pending claims amply satisfy this standard. Applicants contend that one of skill in the art can readily recognize that Applicants invented that which is claimed.

As noted above, the Examiner has based this rejection on case law addressing the requirements for adequately describing a previously unknown biological composition. In contrast, the instant claims are directed to methods of using a biological composition, wherein working examples of the biological composition already existed in the art and were described in the specification. Despite the factual differences between the instant claims and the claims at issue in the cases cited by the Examiner, Applicants have detailed above the numerous ways in which the instant claims even comply with the written description standard reflected in these cases. Thus, contrary to the Examiner's contention, the claimed invention is described in a manner that exceeds that which is required for compliance under 35 U.S.C. 112, first paragraph.

The claims, as amended, are directed to the use of *hedgehog* antibodies that bind Sonic hedgehog protein and inhibit *hedgehog* signaling. The specification and the art teach examples of

such anti-hedgehog antibodies. The sequence and structure of the Sonic hedgehog antigen was well known in the art at the time the instant application was filed. Accordingly, one of skill in the art can readily envision the *hedgehog* antibodies for use in the claimed methods, and Applicants contend that the claims are fully compliant with the written description requirement. Reconsideration and withdrawal of this rejection are requested.

Double Patenting

Claims 1, 3, 5, 21, and 23-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claim 25 of copending application number 10/652,298. Applicants contend that the claims, as amended, in the instant and co-pending applications are patentable in view of each other. Nevertheless, Applicants ask that this rejection be held in abeyance until indication of allowable subject matter. Applicants will submit a terminal disclaimer, if necessary, upon indication of allowable subject matter.

New Objections and/or Rejections

Claim Objections

Claim 1 is objected to because of certain grammatical errors. Applicants have amended claim 1 to correct these grammatical errors. Applicants' amendment is believed to obviate the objection. Applicants' amendment does not alter the scope of the claims.

Claim Rejections – 35 § USC 112, 2nd paragraph

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants traverse this rejection and contend that the rejection is moot in view of the amended claims.

Claim 21 is rejected because recitation of "and/or" allegedly renders the claim unclear. Applicants traverse. Applicants contend that one of skill in the art can readily ascertain the metes and bounds of the claimed subject matter. Nevertheless, to expedite prosecution, Applicants have amended claim 21 to improve its clarity. Applicants' amendment is believed to obviate the

rejection. Applicants' amendment is made solely to expedite prosecution and is not in acquiescence to the rejection. Applicants' amendment is believed to improve the clarity of the claim without altering its scope. Reconsideration and withdrawal of this rejection are requested.

Claim Rejections – 35 § USC 102(b)

Claim 1 is rejected as allegedly anticipated by Wallace et al., 12 April 1999, Current Biology 9: 445-448 ("Wallace"). Applicants traverse this rejection and contend that the rejection is moot in view of the amended claims.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1978). Wallace fails to anticipate the invention as set forth in the present claims.

Wallace examines a role for hedgehog signaling in the postnatal murine cerebellum. Hedgehog signaling was inhibited using an anti-Sonic hedgehog antibody. As specifically pointed out by the Examiner on page 13 of the Office Action, the purpose of the experiments in Wallace was "[t]o determine whether Shh plays a part in normal EGL development." The goal in Wallace was to determine whether Shh signaling was involved in cerebellum development. Wallace showed that inhibiting hedgehog signaling led to thinning of the EGL, indicating that hedgehog signaling was important for at least some aspects of cerebellum development. In other words, treatment with the anti-hedgehog antibody resulted in anomalies in development. Thus, contrary to the position advanced by the Examiner on page 13 of the Office Action, the cell proliferation inhibited by the anti-Shh antibody was not unwanted cell proliferation. Rather, the cell proliferation inhibited by the anti-Shh antibody was actually important for proper development.

In contrast, claim 1 is specifically directed to a method of inhibiting *unwanted cell proliferation*. Given that Wallace teaches a method of inhibiting cell proliferation that is important for normal development, Wallace fails to teach a method of inhibiting unwanted cell proliferation. As such, Wallace fails to teach or suggest each and every element of the claimed invention, and thus fails to anticipate the claimed invention.

Nevertheless to expedite prosecution, Applicants have amended the claims to incorporate the novel and inventive features of claims 3 and 5. Specifically, Applicants have amended the claims to specify that the unwanted cell proliferation is *associated with cancer* and that the cancer is *associated with one or more of prostate, breast, bladder, or colon tissue.* Wallace fails to teach or suggest the study or modulation of cancer tissue, generally. Further, Wallace fails to teach or suggest the study or modulation of cancer associated with prostate, breast, bladder, or colon tissue. Accordingly, Wallace fails to anticipate the claimed invention.

Applicants' amendments are not in acquiescence to the rejection. Applicants reserve the right to prosecute claims of similar or differing scope. Applicants' amendments are believed to obviate the rejection, and reconsideration and withdrawal of this rejection are requested.

Claim Rejections – 35 § USC 103(a)

Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Dahmane #1 in view of Dahmane #2. Applicants traverse this rejection and contend that the rejection is moot in view of the amended claims.

To expedite prosecution, Applicants have amended claim 1 to incorporate the novel and nonobvious features of claim 5, and have cancelled claim 3 to avoid redundancy. Applicants note that claim 5 has not been rejected based on the combined teachings of these references. As amended, claim 1 more particularly points out that the unwanted cell proliferation is *associated with cancer* and that the cancer is *associated with one or more of prostate, breast, bladder, or colon tissue.*

To establish a *prima facie* case of obviousness, the following three criteria must be met: (i) there must be some suggestion or motivation to modify the reference or to combine reference teachings, (ii) there must be a reasonable expectation of success of combining the cited references to arrive at the claimed invention, and (iii) the prior art references must teach or suggest each and every limitation of the claimed invention. MPEP 2142-2143. The combined teachings of Dahmane #1 and Dahmane #2 fail to satisfy any of these criteria, and thus fail to undermine the patentability of the claimed invention.

Applicants' amendments are not in acquiescence to the rejection. Applicants reserve the right to prosecute claims of similar or differing scope. Applicants' amendments are believed to obviate the rejection, and reconsideration and withdrawal of this rejection are requested.

Co-Pending Applications

The Examiner is obviously aware of co-pending application 10/652,298 (currently applied in the above noted double patenting rejection). Applicants direct the Examiner to the prior and ongoing prosecution of co-pending application 10/652,298 (most recent action is a Non-Final Office Action mailed August 22, 2007). Additionally, Applicants take this opportunity to bring the prior and ongoing prosecution of the following co-pending applications to the Examiner's attention: application serial number 09/804,490, application serial number 10/652,686, application serial number 09/883,848, application serial number 10/772,090, and application serial number 10/727,195. Prosecution in these co-pending applications is ongoing. The most recent action in application serial number 09/804,490 is a Notice of Allowance mailed November 7, 2007. The most recent action in application serial number 10/652,686 is a Non-Final Office Action mailed November 2, 2007. The most recent action in application serial number 09/883,848 is a response filed November 30, 2007 (responsive to an action mailed July 10, 2007). The most recent action in application serial number 10/772,090 is a response filed October 22, 2007 (responsive to an action mailed September 20, 2007). The most recent action in application serial number 10/727,195 is a Final Office Action mailed November 9, 2007. Applicants enclose herewith a Supplemental Information Disclosure Statement to make these and other references of record.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945** under order number CIBT-P01-104.

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Respectfully submitted,

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